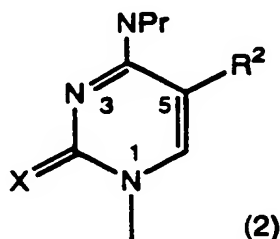
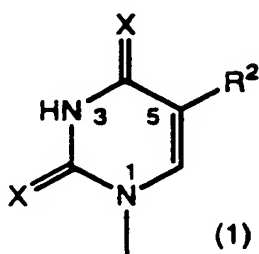


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CLAIMS

1. An oligomer comprising at least two nucleomonomers and pharmaceutically acceptable salts thereof wherein at least one of said nucleomonomers comprises a base of formula (1) or (2):



15

wherein each X is independently O or S;  
R<sup>2</sup> is a group comprising at least one pi bond connected to the carbon atom attached to the base; and  
Pr is (H), or a protecting group,

20

with the proviso that when at least one of said nucleomonomers of said oligomer comprises deoxyuridine 5-substituted by vinyl, 1-butenyl, 1-pentenyl, 1-hexenyl, 1-heptenyl, 1-octenyl, 1-propynyl, 1-butynyl, 1-hexynyl, 1-heptynyl, or 1-octynyl, then the remainder of the nucleomonomers comprising said oligomer are not solely comprised of phosphodiester linked 2'-deoxyadenosine, 2'-deoxyguanosine, 2'-deoxycytidine, thymidine or a combination thereof.

25

30

2. The oligomer of claim 1 wherein X is O.

35

3. The oligomer of claim 1 or 2 wherein R<sup>2</sup> is not phenyl.

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4. The oligomer of claim 1 or 2 wherein R<sup>2</sup> is  
cyano, C<sub>2-12</sub> 1-alkenyl or 1-alkynyl or is a C<sub>2-12</sub>  
heteroaromatic or 1-ethynyl-heteroaromatic group  
containing 5-6 ring atoms in which one to three of the  
5 ring atoms is N, S or O.

5. The oligomer of claim 4 wherein R<sup>2</sup> is C<sub>2-4</sub>  
1-alkenyl or 1-alkynyl or is a C<sub>2-4</sub> heteroaromatic or 1-  
ethynyl-heteroaromatic group containing 5-6 ring atoms in  
10 which one ring atom is replaced by N and optionally in  
which a second ring atom is N, S or O.

6. The oligomer of claim 5 wherein R<sup>2</sup> is  
selected from the group consisting of phenylethynyl, 2-,  
15 3-, and 4-pyridine-ethynyl, 2-, 4- and 5-pyrimidine-  
ethynyl, triazine-ethynyl, 2-pyrimidinyl, 4-pyrimidinyl,  
5-pyrimidinyl, 2-, 4- and 5-oxazolyl-ethynyl, 2-, 4- and  
5-thiazolyl-ethynyl, 1-methyl-2-imidazolyl, 2- and 4-  
imidazolyl, 2-, 4- and 5-oxazolyl, 2-, 4- and  
20 5-imidazolyl-ethynyl, 2-pyridinyl, 3-pyridinyl, 4-  
pyridinyl, 2- and 3-thienyl-ethynyl, 2- and 3-furanyl-  
ethynyl, 2- and 3-pyrrolyl-ethynyl, 2- and 3-thienyl, 2-,  
4-, and 5-oxazolyl, 2- and 3-furanyl, 2- and 3-pyrrolyl,  
propenyl, vinyl and -C≡C-Z where Z is H, alkyl (C<sub>1-10</sub>),  
25 haloalkyl (C<sub>1-10</sub> with 1 to 6 halogen atoms) or heteroalkyl  
(C<sub>1-10</sub> with 1 to 3 heteroatoms).

7. The oligomer of claim 1 wherein R<sup>2</sup> is  
selected from the group consisting of 1-propynyl, 1-  
30 propenyl, 3-buten-1-ynyl, 3-methyl-1-butynyl,  
3,3-dimethyl-1-butynyl, 1,3-pentadiynyl, 1-butynyl,  
ethynyl, vinyl, bromovinyl, phenylethynyl, 2-, 3-, and 4-  
pyridine-ethynyl, 2-, 4- and 5-pyrimidine-ethynyl,  
35

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triazine-ethynyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 2-, 4- and 5-oxazolyl-ethynyl, 2-, 4- and 5-thiazolyl-ethynyl, 1-methyl-2-imidazolyl, 2- and 4-imidazolyl, 2-, 4- and 5-oxazolyl, 2-, 4- and  
5 5-imidazolyl-ethynyl, 2-pyridinyl, 3-pyridinyl, 4-pyridinyl, 2- and 3-thienyl-ethynyl, 2- and 3-furanyl-ethynyl, 2- and 3-pyrrolyl-ethynyl, 2- and 3-thienyl, 2-, 4-, and 5-oxazolyl, 2- and 3-furanyl, and 2- and 3-pyrrolyl.

10

8. The oligomer of claim 1 wherein R<sup>2</sup> is 1-propynyl.

9. The oligomer of claim 8 wherein at least  
15 one substitute linkage is a phosphorothioate linkage.

10. The oligomer of claim 9 wherein all substitute linkages are phosphorothioate linkages.

20

11. The oligomer of claim 1 wherein at least one substitute linkage is a phosphorothioate linkage.

12. The oligomer of claim 11 wherein all substitute linkages are phosphorothioate linkages.

25

13. The oligomer of claim 1 wherein at least one linkage is a substitute linkage.

14. The oligomer of claim 13 wherein the  
30 substitute linkage is selected from the group consisting of phosphoramidate, phosphorothioate, methylphosphonate, riboacetal, amide, N-methylhydroxylamine,

35

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thi n methylphosphonate, phosphorodithioate, 2',5'  
linkages, formacetal, and 3'-thioformacetal.

15       15. The oligomer of claim 14 wherein said  
substitute linkage is methylphosphonate or  
phosphorothioate.

10       16. The oligomer of claim 3 wherein at least  
one substitute linkage is a phosphorothioate linkage.

17. The oligomer of claim 16 wherein all  
substitute linkages are phosphorothioate linkages.

15       18. The oligomer of claim 3 wherein at least  
one linkage is a substituted linkage.

20       19. The oligomer of claim 18 wherein the  
substitute linkage is selected from the group consisting  
of phosphoramidate, phosphorothioate, methylphosphonate,  
riboacetal, amide, N-methylhydroxylamine,  
thionomethylphosphonate, phosphorodithioate, 2',5'  
linkages, formacetal, and 3'-thioformacetal.

25       20. The oligomer of claim 19 wherein said  
substitute linkage is methylphosphonate or  
phosphorothioate.

30       21. The oligomer of claim 1 that further  
comprises at least one segment of inverted polarity.

22. The oligomer of claim 21 that further  
comprises at least one o-xyloso switchback linker.

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23. The oligomer of claim 22 wherein the  
o-xyloso switchback linker comprises at least one base of  
formula (1) or (2) as defined in claim 1.

5           24. The oligomer of claim 1 wherein at least  
one base comprises a covalent bonding moiety.

          25. The oligomer of claim 24 wherein said base  
is N<sup>4</sup>,N<sup>4</sup>-ethanocytosine.

10

          26. The oligomer of claim 1 complexed with a  
cationic lipid.

          27. The oligomer of claim 1 further comprising  
15 from about 10 to about 30 nucleomonomers and having  
uniform polarity.

          28. The oligomer of claim 27 further  
comprising about 2 to about 12 substituted linkages or  
20 nucleomonomers at the 5'- end and at the 3'- end which  
comprise nuclease stable domains, and about 3 to about 26  
substituted linkages or nucleomonomers which comprise at  
least one RNase H competent domain and is between the  
nuclease stable domains.

25

          29. The oligomer of claim 3 complexed with a  
cationic lipid.

          30. The oligomer of claim 3 further comprising  
30 from about 10 to about 30 nucleomonomers and having  
uniform polarity.

35

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31. The oligomer of claim 4 wherein said nucleomonomer is a 2'- modified nucleomonomer.

32. The oligomer of claim 31 wherein at least one of the nucleomonomer is a 2'-O-allyl modified nucleomonomer.

33. The oligomer of claim 1 having a covalent link between the 5' nucleomonomer and the 3' nucleomonomer whereby a circular oligomer is formed.

34. The oligomer of claim 1 conjugated to a solid support, label, or amine linker (1-12C).

35. The oligomer of claim 1 which is a dimer, trimer, tetramer, pentamer or hexamer.

36. The oligomer of claim 3 conjugated to a solid support, label, or amine linker (1-12C).

37. The oligomer of claim 3 which is a dimer, trimer, tetramer, pentamer or hexamer.

38. An oligomer of claim 1 comprising a positive modification comprising at least one base of formula (1) or (2) and a negative modification, with respect to the binding affinity of the oligomer to a complementary nucleic acid sequence, wherein the positive modification counteracts the effect of the negative modification to a degree that is more than additive with respect to the binding affinity.

35

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39. The oligomer of claim 38 wherein the positive modification R<sup>2</sup> is cyano, C<sub>2-12</sub> 1-alkenyl or 1-alkynyl or is a C<sub>2-12</sub> heteroaromatic or 1-ethynyl-heteroaromatic group containing 5-6 ring atoms in which one to three of the ring atoms is independently N, S or O.

40. The oligomer of claim 39 wherein the heterocycle base modification R<sup>2</sup> is C<sub>2-6</sub> 1-alkenyl or 1-alkynyl or is a C<sub>2-6</sub> heteroaromatic or 1-ethynyl-heteroaromatic group containing 5 to 6 ring atoms in which one ring atom is N and optionally in which a second ring atom is N, S or O and each X is O.

41. The oligomer of claim 37 wherein the negative modification is a substitute linkage.

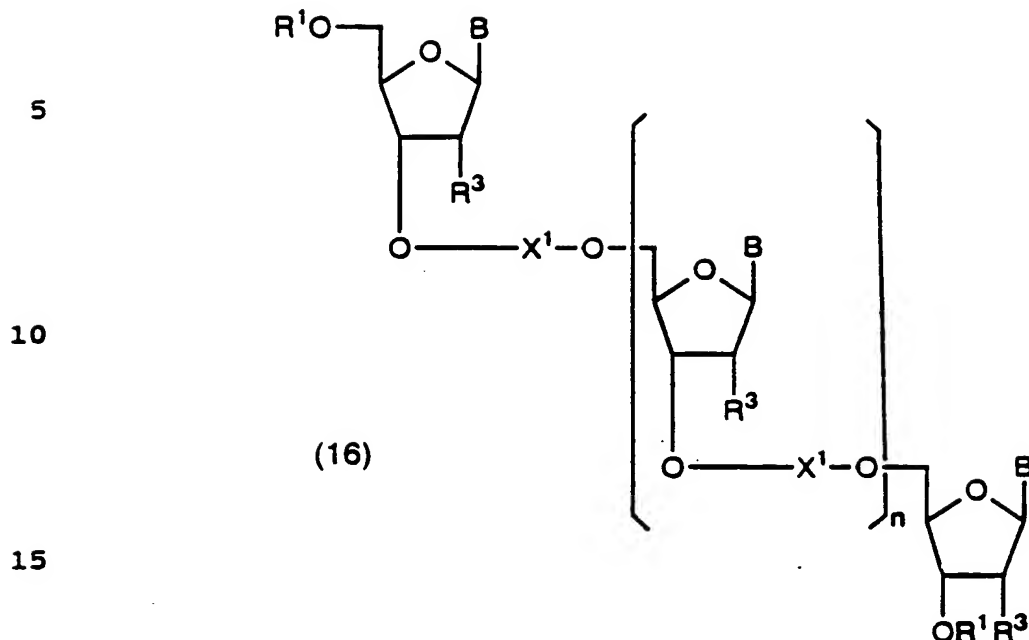
42. The oligomer of claim 41 wherein the substitute linkage comprises at least one linkage selected from the group consisting of phosphorothioate, thionomethylphosphonate, methylphosphonate, phosphoroamidate and triester for a phosphodiester linkage.

43. The oligomer of claim 1 wherein at least one R<sup>3</sup> is O-methyl, O-ethyl or O-propyl.

44. The oligomer of claim 3 wherein at least one R<sup>3</sup> is O-methyl, O-ethyl or O-propyl.

45. An oligomer of the formula (16):

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20 wherein each  $R^1$  is independently H,  $PO_3^{2-}$ , or a blocking group;

each  $R^3$  is independently selected from the group consisting of H, OH, F,  $NH_2$ ,  $OCH_3$ ,  $OC_2H_5$ ,  $OC_3H_7$ ,  $SCH_3$ ,  $SC_2H_5$ ,  $SC_3H_7$ ,  $OC_4H_9$ , and  $SC_4H_9$ ;

25 each  $X^1$  is independently a substitute linkage selected from the group consisting of  $-P(S)(O)-$ ,  $-P(O)(O)-$ ,  $-P(Me)(O)-$  and  $-P(Me)(S)-$ .

Pr is a protecting group;

n is an integer from 0 to 98; and

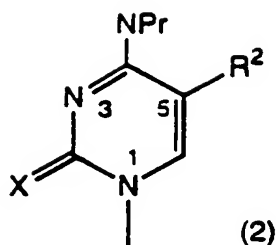
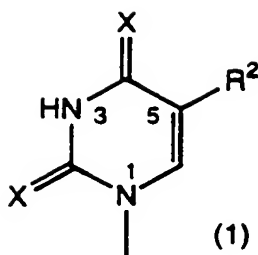
30 B is a purine or pyrimidine base, provided that at least one B is of formula (1) or (2):

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5



10                    wherein each X is independently O or S; R<sup>2</sup>  
is a group comprising at least one pi bond connected  
through a carbon attached to the base; and

                  Pr is H<sub>2</sub> or a protecting group and  
with the proviso that when at least one of said  
15    nucleomonomers of said oligomer comprises deoxyuridine 5-  
substituted by vinyl, 1-butenyl, 1-pentenyl, 1-hexenyl,  
1-heptenyl, 1-octenyl, 1-propynyl, 1-butynyl, 1-hexynyl,  
1-heptynyl, or 1-octynyl, then the remainder of the  
nucleomonomers comprising said oligomer are not solely  
20    comprised of phosphodiester linked 2'-deoxyadenosine, 2'-  
deoxyguanosine, 2'-deoxycytidine, thymidine or a  
combination thereof.

25                    46. The oligomer of claim 45 wherein at least  
one B is 5-propynyluracil, 5-(3-methyl-1-butynyl)uracil,  
5-propynylcytosine or 5-(3-methyl-1-butynyl)cytosine.

30                    47. The oligomer of claim 45 wherein at least  
one B is 2-thienyluracil, 2-thienylcytosine, 2-  
imidazoyluracil, 2-imidazoylcytosine, 2-thiazoyluracil or  
2-thiazoylcytosine.

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48. The oligomer of claim 45 wherein at least one R<sup>1</sup> is H, PO<sub>3</sub><sup>2-</sup>, DMT, MMT, H-phosphonate, methyl phosphonamidite, methylphosphoramidite, β-cyanoethylphosphoramidite or alkylphosphoramidite.

5

49. The oligomer of claim 45 wherein each R<sup>3</sup> is independently H, OH, or -O-allyl.

50. The oligomer of claim 50 wherein at least one R<sup>3</sup> is O-methyl, O-ethyl or O-propyl.

10

51. The oligomer of claim 45 wherein R<sup>2</sup> is 1-propynyl.

15

52. The oligomer of claim 51 further comprising from about 10 to about 30 nucleomonomers and having uniform polarity and further comprising about 2 to about 12 substituted linkages or nucleomonomers at the 5'- end and at the 3'- end which comprise nuclease stable domains, and about 3 to about 26 substituted linkages or nucleomonomers which comprise at least one RNase H competent domain and is between the nuclease stable domains.

20

25

53. The oligomer of claim 45 complexed with a cationic lipid.

30

54. The oligomer of claim 46 wherein the cationic lipid is DOTMA.

55. The oligomer of claim 45 wherein R<sup>2</sup> is not phenyl.

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56. The oligomer of claim 55 wherein at least one  $R^1$  is H,  $PO_3^{2-}$ , DMT, MMT, H-phosphonate, methyl phosphonamidite, methylphosphoramidite,  $\beta$ -cyanoethylphosphoramidite or alkylphosphoramidite.

5

57. The oligomer of claim 55 wherein each  $R^3$  is independently H, OH, or -O-allyl.

58. The oligomer of claim 55 wherein at least one  $R^3$  is O-methyl, O-ethyl or O-propyl.

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59. The oligomer of claim 55 complexed with a cationic lipid.

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60. The oligomer of claim 59 wherein the cationic lipid is DOTMA.

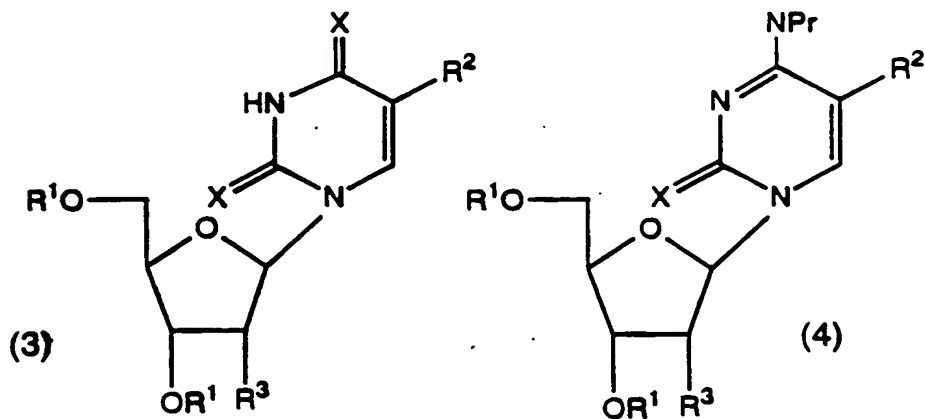
61. A nucleomonomer having the structural formula (3) or (4):

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wherein each R<sup>1</sup> is independently H or a blocking group;

R<sup>2</sup> is a group comprising at least one pi bond connected through a carbon atom attached to the base;

5 Pr is (H)<sub>2</sub> or a protecting group; and

R<sup>3</sup> is selected from the group consisting of H, OH, F, OCH<sub>3</sub>, OC<sub>2</sub>H<sub>5</sub>, OC<sub>3</sub>H<sub>7</sub>, SCH<sub>3</sub>, SC<sub>2</sub>H<sub>5</sub>, SC<sub>3</sub>H<sub>7</sub>, OC<sub>3</sub>H<sub>7</sub>, and SC<sub>3</sub>H<sub>7</sub>,

with the proviso that if R<sup>3</sup> is H or OH, and both R<sup>1</sup> are H, R<sup>2</sup> is 1,3-pentadiynyl, 2-, 3-, and 4-pyridine-ethynyl, 2-pyrimidine-ethynyl, 4-pyrimidine-ethynyl, 5-pyrimidine-ethynyl, triazine-ethynyl, 2-pyrimidinyl, 2- and 4-imidazolyl, 2- and 3-pyrrolyl-ethynyl, 2- and 3-furanyl-ethynyl, 2- and 3-thienyl-ethynyl, 2-, 4- and 5-imidazolyl-ethynyl, 2-, 4-, and 5-thiazolyl-ethynyl, 2-, 4- and 5-oxazolyl-ethynyl, 4- and 5-thiazolyl, 4- and 5-oxazolyl, or 3-pyrrolyl.

62. The nucleomonomer of claim 61 wherein Pr is (H)<sub>2</sub>.

20

63. The nucleomonomer of claim 61 wherein R<sup>2</sup> is 1-propynyl, 1-propenyl, 3-buten-1-ynyl, 3-methyl-1-butynyl, 3,3-dimethyl-1-butynyl, 1,3-pentadiynyl, 1-butynyl, ethynyl, vinyl, bromovinyl, phenylethynyl, 2-, 3-, and 4-pyridine-ethynyl, 2-, 4- and 5-pyrimidine-ethynyl, triazine-ethynyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 2-, 4- and 5-oxazolyl-ethynyl, 2-, 4- and 5-thiazolyl-ethynyl, 1-methyl-2-imidazolyl, 2- and 4-imidazolyl, 2-, 4- and 5-oxazolyl, 2-, 4- and 5-imidazolyl-ethynyl, 2-pyridinyl, 3-pyridinyl, 4-pyridinyl, 2- and 3-thienyl-ethynyl, 2- and 3-furanyl-ethynyl, 2- and 3-pyrrolyl-ethynyl, 2- and 3-thienyl, 2-,

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4-, and 5-oxazolyl, 2- and 3-furanyl, or 2- and 3-pyrrolyl; and

the blocking group is DMT, MMT, FMOC, hydrogen phosphonate, methylphosphonamidite, methylphosphoramidite  
5 or  $\beta$ -cyanoethylphosphoramidite.

64. The nucleomonomer of claim 63 wherein  $R^1$  is H, OH or O-allyl.

10 65. The nucleomonomer of claim 63 wherein  $R^1$  is 1-propynyl.

66. The nucleomonomer of claim 63 wherein  $R^1$  at the 3' position is selected from the group consisting  
15 of hydrogen phosphonate, N,N-diisopropylamino- $\beta$ -cyanoethoxyphosphine, N,N-diisopropyl-aminomethoxyphosphine, N,N-diethylamino- $\beta$ -cyanoethoxyphosphine, N,N-morpholino- $\beta$ -cyanoethoxyphosphine, N,N-morpholinomethoxyphosphine, N,N-diisopropylaminomethyl-  
20 phosphonamidite, N,N-diethylamino-methylphosphonamidite, bis-morpholino-phosphine, N,N-dimethylamino- $\beta$ -cyanoethylmercaptophosphine, 2-chlorophenyl phosphate, 4-chlorophenyl phosphate, 2,4-dichlorophenyl phosphate, 2,4-dibromophenyl phosphate, 2-chlorophenyl  
25 thiophosphate, 4-chlorophenyl thiophosphate, 2,4-dichlorophenyl thiophosphate, and 2,4-dibromophenyl phosphate.

30 67. The nucleomonomer of claim 61 wherein  $R^1$  is 1-propynyl.

68. The nucleomonomer of claim 61 wherein X is  
35 O;

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$R^1$  at the 5' position is DMT, MMT or FMOC;  
 $R^1$  at the 3' position is N,N-diisopropylamino-  
 $\beta$ -cyanoethoxyphosphine, N,N-diisopropylaminomethoxy-  
phosphine or hydrogen phosphonate;

5  $R^2$  is 1-propynyl, 3-methyl-1-butyryl, 2-thienyl, 2-imidazolyl or 2-thiazolyl;

$R^3$  is H, OH, or O-allyl; and

Pr is (H), diisobutylformamidine or another protecting group.

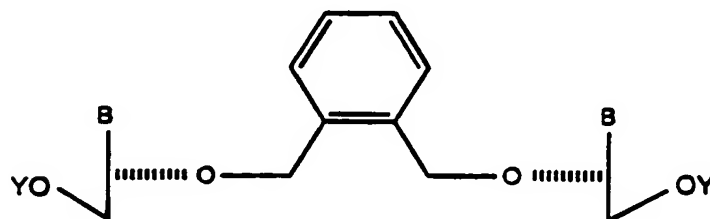
10

69. The nucleomonomer of claim 68 wherein Pr is benzoyl, diisopropylformamidine, FMOC, di-n-butylformamidine, or isobutyryl.

15

70. An o-xyloso dimer of the formula (5):

20



(5)

25 wherein

each Y is independently  $R^1$  or an oligomer;

$R^1$  is H,  $PO_3^{2-}$  or a blocking group; and

30 each B is independently a purine or pyrimidine base, provided that at least one B is a base of formula (1) or (2), wherein  $R_2$  is a group comprising at least one pi bond connected through a carbon atom attached to the base; and Pr is (H), or a protecting group.

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71. The dimer of claim 70 wherein R<sup>1</sup> is 1-propynyl.

72. The dimer of claim 70 wherein the blocking group is selected from the group consisting of DMT, MMT, hydrogen phosphonate, methylphosphonamidite, methylphosphoramidite, and  $\beta$ -cyanoethylphosphoramidite.

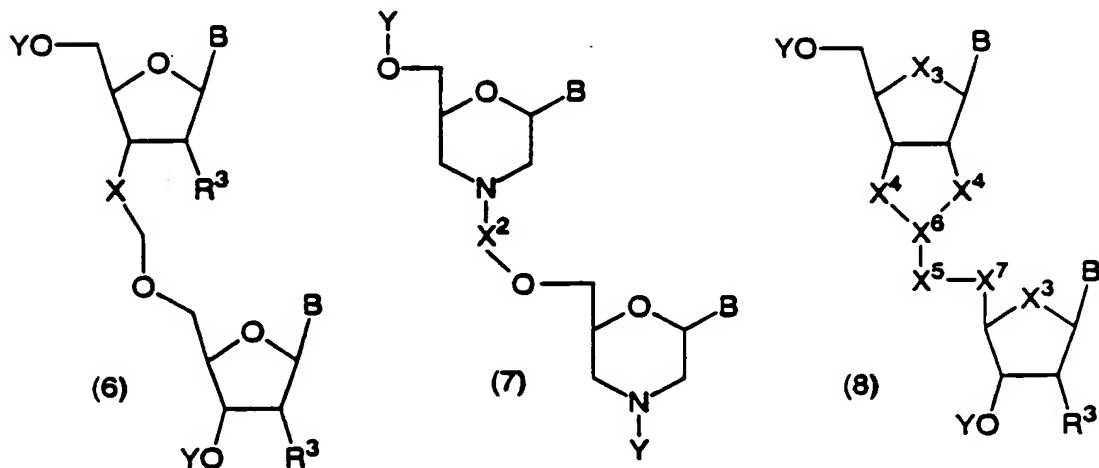
73. A dimer of the formula (6), (7) or (8):

10

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25



wherein

X is selected from the group consisting of O and S;

30 X<sup>1</sup> is selected from the group consisting of CO, CS and SO<sub>2</sub>;

35 X<sup>3</sup> is independently selected from the group consisting of O, S, CH<sub>2</sub>, CF<sub>2</sub> and CFH;

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$X^4$  is independently selected from the group consisting of O, S, SO, SO<sub>2</sub>, CH<sub>2</sub>, CO, CF<sub>2</sub>, CS, NH and NR<sup>4</sup> wherein R<sup>4</sup> is lower alkyl (C<sub>1-4</sub>; methyl, ethyl, propyl, isopropyl, butyl or isobutyl);

5  $X^5$  is selected from the group consisting of O, CO, S, CH<sub>2</sub>, CS, SO<sub>2</sub>, CO, NH and NR<sup>4</sup>;

$X^6$  is selected from the group consisting of CH, N, CF, CCl, and CR<sup>5</sup> wherein R<sup>5</sup> is lower alkyl (C<sub>1-4</sub>) fluoromethyl, difluoromethyl, trifluoromethyl or lower  
10 fluoroalkyl (C<sub>2-4</sub>, F<sub>1-3</sub>);

$X^7$  is selected from the group consisting of O, S, CH<sub>2</sub>, CO, CF<sub>2</sub> and CS;

each Y independently is an oligomer or R<sub>1</sub> wherein R<sub>1</sub> is PO<sub>3</sub><sup>-2</sup> or a blocking group;

15 each R<sup>3</sup> is independently selected from the group consisting of H, OH, F, NH<sub>2</sub>, OCH<sub>3</sub>, OC<sub>2</sub>H<sub>5</sub>, OC<sub>3</sub>H<sub>7</sub>, SCH<sub>3</sub>, SC<sub>2</sub>H<sub>5</sub>, SC<sub>3</sub>H<sub>7</sub>, OC<sub>3</sub>H<sub>7</sub>, and SC<sub>3</sub>H<sub>7</sub>;

each B is independently a purine or pyrimidine base, provided that at least one B is of formula (1) or  
20 (2) wherein each X is O or S;

R<sub>2</sub> is a group comprising at least one pi bond connected through a carbon atom attached to the base; and  
Pr is (H)<sub>2</sub> or a protecting group;

25 and further provided that X<sup>5</sup> and X<sup>7</sup> are not both O.

74. The dimer of claim 73 wherein R<sup>1</sup> is PO<sub>3</sub><sup>-2</sup>, DMT, MMT, H-phosphonate, methylphosphoramidite or  
30  $\beta$ -cyanoethylphosphoramidite.

75. The dimer of claim 73 wherein at least one B is 5-propynyluracil, 3-methyl-1-butynyluracil, 5-  
35 propynylcytosine, or 3-methyl-1-butynylcytosine.



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76. The dimer of claim 73 wher in at least one R<sup>2</sup> is propynyl, R<sup>3</sup> is H or OH and X in the substitute linkage is S.

5           77. The dimer of claim 73 of formula (8) wherein X<sup>3</sup> and X<sup>4</sup> are O, X<sup>5</sup> and X<sup>7</sup> are CH<sub>2</sub>, and X<sup>6</sup> is CH.

78. A duplex wherein one of the two oligomers of the duplex is comprised of an oligomer of claim 1.

10

79. A duplex wherein one of the two oligomers of the duplex is comprised of an oligomer of claim 45.

80. A triplex wherein one of the three oligomers of the triplex is comprised of the oligomer of claim 1.

15

81. A triplex wherein one of the three oligomers of the triplex is comprised of the oligomer of claim 45.

20

82. A duplex wherein one of the two oligomers of the duplex is comprised of an oligomer of claim 3.

83. A duplex wherein one of the two oligomers of the duplex is comprised of an oligomer of claim 55.

25

84. A triplex wherein one of the three oligomers of the triplex is comprised of the oligomer of claim 3.

30

35

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85. A triplex wherein one of the three oligomers of the triplex is comprised of the oligomer of claim 55.

5           86. The oligomer of claim 1 wherein the oligomer persists intact in cells or biological solutions for a period of time that is greater than a corresponding oligodeoxynucleotide.

10           87. The oligomer of claim 3 wherein the oligomer persists intact in cells or biological solutions for a period of time that is greater than a corresponding oligodeoxynucleotide.

15           88. The oligomer of claim 1 wherein the oligomer is a ribozyme.

            89. The oligomer of claim 3 wherein the oligomer is a ribozyme.

20           90. The oligomer of claim 1 wherein the oligomer is a probe.

            91. The oligomer of claim 3 wherein the oligomer is a probe.

            92. The oligomer of claim 1 wherein the oligomer is a primer.

30           93. The oligomer of claim 3 wherein the oligomer is a primer.

35           94. A pharmaceutical composition, comprising:

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a pharmaceutically acceptable carrier; and  
a therapeutically effective amount of an  
oligomer of claim 1.

5           95. A method of treating a disease in a  
subject, which disease is characterized by a particular  
DNA duplex or RNA, comprising the steps of:

          administering to a subject in need of such  
treatment a therapeutically effective amount of an  
10   oligomer of claim 1; and

          allowing the oligomer to have sufficient time  
to bind to the DNA duplex or RNA.

          96. A method of treating a disease in a  
15   subject, which disease is characterized by a particular  
DNA or RNA, the method comprising:

          administering to a subject in need of such  
treatment a therapeutically effective amount of an  
oligomer of claim 1; and

20           allowing the oligomer to have sufficient time  
to bind to the DNA or RNA to form a triplex or duplex.

          97. A method of detecting the presence,  
absence or amount of a particular double stranded or  
25   single stranded nucleic acid in a biological sample,  
comprising the steps of:

          contacting the sample with an oligomer of claim  
1 under conditions wherein a duplex or a triplex is  
formed between the oligomer and the nucleic acid; and

30           detecting the presence, absence or amount of  
said duplex or triplex.

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98. A method of detecting the presence ,  
absence or amount of a particular single-stranded DNA or  
RNA in a biological sample, comprising the steps of:

5       contacting the sample with an oligomer of claim  
1 under conditions wherein a hybrid duplex is formed  
between the oligomer and the DNA or RNA; and  
      detecting the presence, absence or amount of  
said duplex.

10       99. A method of inhibiting expression of at  
least one selected protein in a cell wherein the protein  
is encoded by DNA sequences and the protein is translated  
from RNA sequences, comprising the steps of:

15       introducing an oligomer of claim 1 into the  
cell; and

      permitting the oligomer to form a triplex with  
the DNA or RNA or a duplex with the DNA or RNA whereby  
expression of the protein is inhibited.

20       100. The method of claim 99 wherein the  
oligomer is introduced into the cell by a method selected  
from the group consisting of calcium phosphate  
transfection, DMSO transfection, dextran transfection,  
electroporation, cationic lipid transfection, anionic  
25   lipid transfection or liposome transfection.

      101. A method of introducing an oligomer of  
claim 1 into cells, comprising:

30       mixing the oligomer with a permeation enhancing  
agent to form a complex; and  
      contacting the complex with the cells.

35       102. A pharmaceutical composition, comprising:

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a pharmaceutically acceptable carrier; and  
a therapeutically effective amount of an  
oligomer of claim 3.

5           103. A method of treating a disease in a  
subject, which disease is characterized by a particular  
DNA duplex or RNA, comprising the steps of:  
          administering to a subject in need of such  
treatment a therapeutically effective amount of an  
10   oligomer of claim 3; and  
          allowing the oligomer to have sufficient time  
to bind to the DNA duplex or RNA.

          104. A method of treating a disease in a  
15   subject, which disease is characterized by a particular  
DNA or RNA, the method comprising:  
          administering to a subject in need of such  
treatment a therapeutically effective amount of an  
oligomer of claim 3; and  
20           allowing the oligomer to have sufficient time  
to bind to the DNA or RNA to form a triplex or duplex.

          105. A method of detecting the presence,  
absence or amount of a particular double stranded or  
25   single stranded nucleic acid in a biological sample,  
comprising the steps of:  
          contacting the sample with an oligomer of claim  
3 under conditions wherein a duplex or a triplex is  
formed between the oligomer and the nucleic acid; and  
30           detecting the presence, absence or amount of  
said duplex or triplex.

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106. A method of detecting the presence, absence or amount of a particular single-stranded DNA or RNA in a biological sample, comprising the steps of:

5       contacting the sample with an oligomer of claim 3 under conditions wherein a hybrid duplex is formed between the oligomer and the DNA or RNA; and  
      detecting the presence, absence or amount of said duplex.

10       107. A method of inhibiting expression of at least one selected protein in a cell wherein the protein is encoded by DNA sequences and the protein is translated from RNA sequences, comprising the steps of:

15       introducing an oligomer of claim 3 into the cell; and  
      permitting the oligomer to form a triplex with the DNA or RNA or a duplex with the DNA or RNA whereby expression of the protein is inhibited.

20       108. The method of claim 107 wherein the oligomer is introduced into the cell by a method selected from the group consisting of calcium phosphate transfection, DMSO transfection, dextran transfection, electroporation, cationic lipid transfection, anionic  
25       lipid transfection or liposome transfection.

      109. A method of introducing an oligomer of claim 1 into cells, comprising:

30       mixing the oligomer with a permeation enhancing agent to form a complex; and  
      contacting the complex with the cells.

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110. A method of introducing an oligomer of claim 3 into cells, comprising:

mixing the oligomer with a permeation enhancing agent to form a complex; and

5           contacting the complex with the cells.

111. A method of synthesizing a desired oligomer of claim 1, comprising the steps of:

10           synthesizing a protected nucleomonomer synthon having a protecting group and a base and further having a coupling group capable of coupling to a nucleomonomer or oligomer;

coupling the nucleomonomer synthon to an acceptor nucleomonomer or an acceptor oligomer;

15           removing the protecting group; and

repeating the cycle as needed until the desired oligomer is synthesized.

112. A method of synthesizing a desired oligomer of claim 1, comprising the steps of:

20           synthesizing a protected oligomer synthon having a protecting group and a base and further having a coupling phosphite or phosphate group capable of coupling to a nucleomonomer or oligomer;

25           coupling the oligomer synthon to an acceptor nucleomonomer or an acceptor oligomer;

removing the protecting group; and

repeating the cycle as needed until the desired oligomer is synthesized.

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113. The method of claim 111 wherein the coupling step is accomplished using hydrogen phosphonate, amidite or triester chemistry.

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114. The method of claim 111 wherein the coupling phosphite or phosphate group is selected from the group consisting of hydrogen phosphonate, N,N-diisopropylamino-methylphosphonamidite, N,N-diethylmethylamino-phosphonamidite, N,N-diisopropylamino- $\beta$ -cyanoethoxyphosphine, N,N-diisopropylamino-methoxyphosphine, N,N-diethylamino- $\beta$ -cyanoethoxyphosphine, N,N-morpholino- $\beta$ -cyanoethoxyphosphine, N,N-morpholino-methoxyphosphine, 2-chlorophenyl phosphate, 4-chlorophenyl phosphate, 2,4-dichlorophenyl phosphate, 2-chlorophenyl thiophosphate, 4-chlorophenyl thiophosphate, 2,4-dichlorophenylthiophosphate, and 2,4-dibromophenyl phosphate.

115. A method to synthesize a derivatized oligomer of claim 1 which comprises:

reacting an oligomer containing at least one 5-iodouracil, 5-iodocytosine or N<sup>4</sup>-protected-5-iodocytosine heterocycle with R<sup>2</sup>H in the presence of a Pd catalyst so as to convert said 5-iodouracil, 5-iodocytosine or N<sup>4</sup>-protected-5-iodocytosine to the corresponding 5-R<sup>2</sup> substituted heterocycle.

116. A method of synthesizing a derivatized oligomer of claim 1, comprising the steps of:

synthesizing a protected precursor nucleomonomer synthon having a protecting group and 5-iodouracil or N<sup>4</sup>-protected-5-iodocytosine as a base;  
coupling the protected precursor nucleomonomer synthon to an acceptor nucleomonomer or an acceptor oligomer;  
removing the protecting group;

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repeating the cycle as needed until the oligomer is synthesized; and

derivatizing the precursor nucleomonomer synthon in said oligomer to a derivative having  $R^2$  at the 5-position, where  $R^2$  has the meaning defined in claim 1.

117. A method to evaluate a candidate antisense oligomer for its ability to inhibit gene expression, which method comprises

10 microinjecting said candidate antisense oligomer into a recombinant host cell along with (a) a target vector for the expression of a gene containing a target sequence for said candidate antisense oligomer, and (b) with a control vector for the expression of a control gene encoding a detectable protein, wherein said control gene does not contain said target sequence.

118. The method of claim 117 wherein said target vector is injected at about 2-4 copies per cell and said control vector is injected at about 30-50 copies per cell.

119. The method of claim 117 wherein said detectable protein is chloramphenicol acetyl transferase, luciferase or  $\beta$ -galactosidase.

120. The method of claim 117 wherein said host cell is a mammalian cell.

121. A host cell which has been microinjected with (a) a target vector containing an expression system for a gene containing a target sequence for an antisense

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ligomer, (b) a control vector containing an expression system for a detectable protein, and (c) a candidate antisense oligomer.

5                   122. A method of amplifying nucleic acid  
comprising the steps:  
                  mixing the oligomer of claim 1 with a sample  
                  containing target nucleic acid;  
                  hybridizing the oligomer with the target  
10   nucleic acid; and  
                  amplifying the target nucleic acid by PCR or  
LCR.

                  123. A method of amplifying nucleic acid  
comprising the steps:  
15                   mixing the oligomer of claim 3 with a sample  
containing target nucleic acid;  
                  hybridizing the oligomer with the target  
nucleic acid; and  
                  amplifying the target nucleic acid by PCR or  
20   LCR.

                  124. The oligomer of claim 1 wherein the  
oligomer is an antisense oligomer.

25                   125. The oligomer of claim 3 wherein the  
oligomer is an antisense oligomer.

                  126. The oligomer of claim 1 wherein the  
oligomer is a triple helix oligomer.  
30

                  127. The oligomer of claim 3 wherein the  
oligomer is a triple helix oligomer.

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